EFFECT OF RAPID WEIGHT LOSS WITH SUPPLEMENTED FASTING ON SERUM ELECTROLYTES, LIPIDS, AND BLOOD PRESSURE

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The effect of rapid weight reduction with supplemented fasting was studied in a group of 46 individuals with moderate to severe obesity. The preparation used contained a mixture of protein, carbohydrate, and essential fatty acids providing 420 kcal daily. It was supplemented with a complement of electrolytes, minerals, and vitamins.

Serum concentrations of electrolytes, urea nitrogen, creatinine, uric acid, glucose, cholesterol, and triglycerides were measured prior to the onset of the study and at two-week intervals for a six-week study period. In addition, blood pressure, heart rate, and body weight were recorded regularly. A mild and transient fall in serum bicarbonate concentration and a rise in uric acid level was observed.

In contrast to other regimens, hypokalemia was not observed in the present study. In fact, serum K+ concentration rose slightly while serum Na+ concentration remained virtually unchanged. There was a transient rise in serum creatinine concentration followed by a fall to values below the baseline. Serum glucose, cholesterol and triglyceride levels, blood pressure, and heart rate decreased significantly. Body weight fell from 232.7 ± 58 lb at the onset of the study to 176.4 ± 47.9 lb at the conclusion of the study.

The protocol was well tolerated and the side effects were mild and infrequent. In conclusion, the present protocol provides a safe and effective means for rapid weight reduction in individuals with moderate to marked obesity without producing severe electrolyte disturbances seen with other modalities.

Obesity is a common disorder that may lead to various complications including hypertension, congestive heart failure, diabetes mellitus, and ischemic heart disease.[1-4] A variety of treatment modalities have been employed to control obesity, with variable results. Supplemented fasting has been widely used in the management of morbid obesity. Although initial attempts were fraught with severe complications, including deaths,[5] recent trials of the modified regimens have proven to be safe and effective.[6-8] In this paper the findings of a survey of serum lipids, electrolytes, and blood pressure in 46 patients treated with supplemented fasting are reported.

METHODS

Patients

Forty-six obese individuals (37 women and 9 men) with a mean age of 41 years were included in the study (Table 1). The patients were accepted only if

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TABLE 1. DESCRIPTIVE CHARACTERISTICS OF STUDY GROUP (n = 46)

Characteristic	Measurement
Sex	
Male (%)	19.6 (n = 9)
Female (%)	80.4 (n = 37)
Mean age (yrs)	41.4 (SD = 10.7)
Mean initial weight (lb)	232.7 (SD = 57.9)

referred by a physician. An informed consent was obtained prior to enrollment into the program. The criteria for participation in the study included severe obesity, ie, body weight at least 25 percent greater than the calculated ideal value. Individuals with type I diabetes mellitus, previous history of hepatocellular disease, cardiovascular disease, alcoholism, renal failure, drug addiction, and psychiatric disorders were excluded from the study.

Before being placed on the dietary regimen, all patients had normal results on the following tests: liver function tests, complete blood count, urinalysis, blood urea nitrogen (BUN), creatinine, electrolytes, uric acid, thyroid function tests, chest roentgenogram, and electrocardiogram.

Protocol

Patients were placed on a controlled diet (Optifast, Sandoz Nutrition Corp, Minneapolis, Minn) consisting of carbohydrate 30 g, protein 70 g, and essential fatty acids 2 g providing 420 kcal per day. The principal ingredients included calcium caseinate, egg white solids, corn syrup solids, lecithin, and partially hydrogenated soybean oil (Table 2). All conventional foods were discontinued, and the diet was supplemented with 600 mg of calcium, 600 mg of potassium chloride, 350 mg of phosphorus, 150 mg of magnesium, and a complement of various vitamins, minerals, and trace elements to prevent deficiency states. It should be noted that the safety of this regimen had been previously verified in a large series of patients.[6-8] The participants were given a one-week supply of the dietary compound at the onset of the program and were instructed to return once a week for additional supplies as well as clinical evaluation. They were highly motivated and compliant and, in fact, paid to participate in the program. The participants were strongly advised against alcohol consumption during the study period and did not take any medications.

The initial clinical evaluation included a complete medical history, physical examination, and aforementioned laboratory tests. Subsequent to the institution of the supplemented fasting protocol, the patients were evaluated and body weight, vital signs, and results of the above laboratory tests were recorded every two weeks for the duration of the program. Dietary regimen was continued for six weeks, after which the patients were tapered off the diet.

Statistical Analysis

The data are presented as mean ± SD. Data analyses were performed on a mainframe computer using the SPSS statistical package.[9] Change over time in serum chemical values, weight loss, blood pressure, and heart rate was evaluated by means of repeated measures, multiple analysis of variance (MANOVA).[10] The MANOVA evaluated within subjects vs between individual changes. It tested the null hypothesis that there were no differences between the mean scores at each observation period of the study. A significant F value indicated that changes over time were greater than variation within individuals and suggested that a significant trend existed in the data. An additional contrast analysis was performed to determine whether individual cell means for any single observation period differed significantly from the remaining cells for the other observation periods. For the contrast analysis a significant F value indicated that a particular cell mean differed significantly from all other cell means.

RESULTS

Body Weight

Body weight prior to the onset of the diet (baseline) was 232.7 ± 58.0 lb. Weight loss occurred throughout the observation period but was greatest between the fourth and sixth weeks ($P < .001$) (Table 3). Body weight at the conclusion of the study was 176.4 ± 47.9 lb, representing a significant reduction as compared with the baseline value ($P < .001$).

TABLE 2. NUTRIENT BREAKDOWN OF OPTIFAST 70

Nutrients	Unit of Measurement	0.86 oz Powder* (1 serving)	Amino Acid Content (g per 100 g protein)	
Protein	g	14		
Carbohydrate	g	6.0	**Essential Amino Acids**	
Fat	g	less than 1 g		
Calories		80	L-Isoleucine	5.45
Vitamin A	IU	1000	L-Leucine	9.28
Vitamin D	IU	80	L-Lysine	7.52
Vitamin E	IU	6.0	L-Methionine	3.02
Vitamin C	mg	18	L-Phenylalanine	5.44
Folic acid	mg	0.08	L-Treonine	4.24
Thiamine	mg	0.45	L-Tryptophan	1.26
Riboflavin	mg	0.52	L-Valine	6.52
Niacin	mg	4.0		
Vitamin B_6	mg	0.60	**Nonessential Amino Acids**	
Vitamin B_{12}	μg	1.2		
Biotin	mg	0.072	L-Alanine	3.91
Pantothenic acid	mg	2.0	L-Arginine	4.21
Calcium	g	0.2	L-Aspartic acid	7.17
Phosphorus	g	0.2	L-Cystine	0.81
Iodine	μg	30	L-Glutamic acid	20.58
Iron	mg	3.6	Glycine	2.43
Magnesium	mg	80	L-Histidine	2.67
Copper	mg	0.40	L-Proline	11.00
Zinc	mg	3.0	L-Serine	6.37
Potassium	mg	390	L-Tyrosine	5.23
Sodium	mg	180		
Manganese	mg	0.80		
Selenium	μg	30		
Chromium	μg	30		
Molybdenum	μg	60		
Vitamin K	μg	20		
Choline	mg	20		
Chloride	mg	0.44		

* 0.88 oz powder per serving for chocolate flavor only.
Each subject received five packets (either vanilla or chocolate) per day at four-hour intervals.
Composition (vanilla flavor): Calcium caseinate, fructose, pasteurized egg white, sugar, potassium citrate, monoammonium phosphate, nonfat dry milk, salt, artificial flavor, corn syrup solids, lecithin, calcium phosphate, mono- and diglycerides, magnesium oxide, choline bitartrate, partially hydrogenated soybean oil, sodium caseinate, high selenium yeast, ascorbic acid, ferrous sulfate, high chromium yeast, aspartame, zinc sulfate, alpha tocopheryl acetate, niacinamide, copper gluconate, manganese sulfate, d-calcium pantothenate, vitamin K, pyridoxine, hydrochloride, riboflavin, vitamin A palmitate, thiamine hydrochloride, folic acid, d-biotin, potassium iodide, sodium molybdate, vitamin D, cyanocobalamin.

Glucose, Uric Acid, and Electrolytes

Changes of serum electrolyte concentrations are shown in Table 3. Serum levels of sodium, potassium chloride, and bicarbonate were within the normal limits at the onset of the study. A statistically significant decrease ($P < .001$) from baseline level occurred at the end of the second week for serum bicarbonate concentration. Thereafter, the values began to rise approaching baseline values six weeks after the onset of the study. The minimum serum bicarbonate level calculated as the mean of the lowest values observed in each individual studied was 20.2 ± 3.8 mEq/L, representing a significant fall ($P < .001$) as compared with the baseline value. The anion gap increased from a normal baseline value to its peak value at four weeks. Thereafter, the anion gap began to fall but remained above the baseline level by the sixth week. The observed trend was highly consistent and statistically significant ($P < .001$). The peak anion gap attained

TABLE 3. CHANGES IN BODY WEIGHT, SERUM ELECTROLYTES, BUN, CREATININE, URIC ACID, AND GLUCOSE IMMEDIATELY BEFORE THE INSTITUTION OF DIET (BASELINE) AND AT TWO, FOUR, AND SIX WEEKS (n = 46)

	Study Period			
Measurement	**Baseline**	**2 weeks**	**4 weeks**	**6 weeks**
Wt (lb)	232.7 (±57.9)	219.2 (±52.9)	209.5 (±50.9)	176.4 (±47.9)
Sodium*	139.6 (±3.0)	139.1 (±2.8)	140.3 (±3.8)	139.8 (±3.0)
Potassium chloride*	4.0 (±0.4)	4.3 (±0.4)	4.2 (±0.3)	4.3 (±0.4)
Bicarbonate*	24.9 (±3.2)	21.8 (±2.8)	22.6 (±3.3)	23.2 (±4.3)
BUN**	14.2 (±3.1)	14.2 (±3.4)	13.2 (±3.4)	13.6 (±4.2)
Creatinine**	0.9 (±0.2)	1.0 (±0.2)	0.9 (±0.2)	0.9 (±0.2)
Uric acid**	5.0 (±1.7)	5.8 (±2.1)	4.8 (±1.4)	4.3 (±1.2)
Glucose**	99.2 (±22.5)	84.5 (±12.22)	85.5 (±13.4)	89.3 (±12.8)

* mEq/L.
** mg/dL.

during the study period (calculated from the highest values observed) was 18.2 ± 4.0 mEq/L, representing a significant increase as compared with the baseline values ($P < .001$). As expected, the changes in serum bicarbonate concentration were inversely related to the changes in the anion gap. Interestingly, the degree of the observed alterations in these measurements did not significantly correlate with the magnitude of weight reduction.

Serum potassium concentration showed a mild but significant rise ($P < .005$) within the normal range. This change became evident at the second week and persisted throughout the study period. Serum sodium concentration remained virtually unchanged throughout the study period. Although serum calcium and inorganic phosphorus concentrations rose slightly during the study period, the observed changes were not considered significant.

Fasting serum glucose concentration was within the normal range at the onset of the study and fell significantly ($P < .0001$) by the second week. It then rose slightly during the remainder of the study period but always remained significantly below the baseline level. These alterations were not proportional to the magnitude of weight reduction.

A significant increase in serum uric acid ($P < .001$) was observed at two weeks but was followed by a decline to values below the baseline levels. Although statistically significant, the mean value for the highest uric acid levels observed during the observation period (6.0 ± 1.9 mg/dL) did not appear to be of clinical significance. Values exceeding 9 mg/dL were observed in two patients.

BUN and Creatinine Levels

Changes in BUN and serum creatinine concentrations are shown in Table 3. There was a slight but nonsignificant decrease in BUN concentration during the study period. In contrast, serum creatinine showed a significant rise at the end of the second week, after which it began to decline, reaching a value slightly below the baseline level at the end of the observation period. This trend was statistically significant ($P < .001$).

Serum Lipids, Blood Pressure, and Pulse Rate

Both serum triglycerides and cholesterol values decreased during the study period. Serum cholesterol reached its nadir at the end of four weeks ($P < .001$). Serum triglyceride levels declined significantly ($P < .001$) throughout the study, with the lowest value recorded at the end of the sixth week. Systolic and diastolic blood pressure at the onset of the study were 141 ± 17 mmHg and 90 ± 10 mmHg, respectively. Both systolic and diastolic blood pressures fell significantly ($P < .001$) during the study period, with the lowest values recorded at the end of the sixth week. Similarly, the pulse rate decreased significantly ($P < .001$), with the lowest values recorded at the end

TABLE 4. CHANGES IN BLOOD PRESSURE (BP), PERIPHERAL PULSE RATE, SERUM CHOLESTEROL, AND SERUM TRIGLYCERIDE LEVELS IMMEDIATELY BEFORE THE INSTITUTION OF DIET (BASELINE) AND AT TWO, FOUR, AND SIX WEEKS (n = 46)

	Study Period			
Measurement	**Baseline**	**2 weeks**	**4 weeks**	**6 weeks**
Systolic BP mmHg	141 ± 18	127 ± 18	125 ± 10	118 ± 20
Diastolic BP mmHg	90 ± 10	81 ± 10	81 ± 5	78 ± 6
Mean arterial pressure	106.9 ± 11.4	96.5 ± 11.5	95.6 ± 5.8	91.1 ± 9.4
Pulse rate counts/min	80 ± 11	74 ± 9	72 ± 7	68 ± 8
Cholesterol mg/dL	228.6 ± 53.6	177.7 ± 53.7	167.4 ± 45.0	195.4 ± 45.3
Triglyceride mg/dL	167.7 ± 87.1	114.8 ± 48.6	113.6 ± 48.4	113.8 ± 53.0

of the study. No significant correlation was found between the alterations in blood pressure, cholesterol, and triglyceride measurements with changes in body weight. These findings are shown in Table 4.

Symptoms

Side effects were of minimal severity and prevalence and consisted largely of dizziness (39.1 percent), constipation (17.4 percent), and muscle cramps (10.9 percent).

DISCUSSION

The present study substantiates the efficacy of supplemented fasting in the treatment of moderate to severe obesity. At six weeks the mean weight loss was 56.3 lb, representing an average loss of 1.3 lb per day. The observed weight loss was associated with a significant fall in serum cholesterol and triglyceride levels. Serum triglyceride levels decreased steadily during the study period to 68 percent of the baseline value in six weeks. Mean serum cholesterol value fell to less than 200 mg/dL after two weeks and remained below the baseline value throughout the study. These findings are in agreement with those described in a number of other reports.[11-14] Contrary to these observations, Palgi et al[15] have shown an increase in serum cholesterol following weight reduction in their female subjects. Of the 37 women evaluated in the study reported herein, only five showed a modest rise in serum cholesterol values, while the majority exhibited a substantial fall. In fact, the mean serum cholesterol value in these 37 women fell by 13.3 percent after six weeks of dietary restriction, demonstrating the hypocholesterolemic effect of this regimen in both sexes.

The reduction in body weight was accompanied by a significant fall in blood pressure. This finding confirms earlier reports that demonstrated a decrease in blood pressure with weight loss without the use of antihypertensive medications.[11-13,15,16] Several mechanisms have been proposed to explain this phenomenon. Decreased salt intake was proposed by Dahl et al,[17] in 1958, to be the major factor in lowering blood pressure during weight loss; however, more recent data have shown that blood pressure can fall despite sodium supplementation.[18] A fall in plasma renin activity (PRA) with weight loss has been demonstrated by several investigators[16,19,20] and has been proposed to contribute to the observed hypotensive effects. Controversy exists as to the role of aldosterone, since some authors have shown parallel reduction in plasma aldosterone concentration and PRA[16] while others have noted a dissociation between the two measurements.[19,20] Increased sympathetic tone has been implicated in the pathogenesis of hypertension associated with obesity. In fact, plasma norepinephrine and epinephrine levels are elevated in obesity and fall with weight reduction.[21,22] Thus the hypotensive effect of weight loss could be in part the result of attenuation of the cardiovascular effects of the catecholamines as well as a decrease in catecholamine-mediated renin release.

Previous reports of deaths associated with very low caloric diets, especially those of poor biological quality protein and little or no mineral and vitamin supplements, implicated electrolyte disturbances as a likely

cause of life-threatening arrhythmias. Frank et al[5] have described overt hypokalemia in a large number of patients treated in this manner. With adequate potassium supplementation, however, hypokalemia did not occur in the study patients. In fact, serum potassium rose slightly during the study period. A number of factors may have been responsible for the observed rise in serum potassium. Mild metabolic acidosis, from starvation ketosis, hypoinsulinemia associated with fasting, and the previously reported fall in plasma catecholamines[21,22] can promote extracellular distribution of this cation and thereby contribute to a rise in its serum concentration. Likewise the catabolic state associated with severe caloric restriction may further contribute to the release of potassium to the extracellular space. These changes along with the substantial K+ supplementation employed in the present regimen and the reported fall in renin and aldosterone levels,[16] which can limit urinary K+ excretion, may account for the mild rise in serum K+ observed in the present study.

The observed reduction in serum bicarbonate level and the accompanying rise in anion gap noted in the study patients signify a metabolic acidosis caused by starvation ketosis. This was clearly mild and required no intervention. The magnitude of the observed changes was greatest early in the course of the study with a gradual return toward normal values achieved by the end of the sixth week. Hyperuricemia seen in this study confirms earlier reports by other investigators[23] and is presumed to be the result of reduced renal excretion of uric acid caused by competition of ketoacids for its tubular transport.[14]

Fasting serum glucose level was within the normal range prior to the onset of the study and significantly decreased during the study period. Similar observations have been made previously and supplemental fasting has been used in the treatment of overweight patients with type II diabetes.[6] Although the precise mechanism responsible for this phenomenon is not known, considerable evidence demonstrated the association of obesity with insulin resistance and compensatory hyperinsulinism. Accordingly, weight reduction restores insulin sensitivity and thereby lowers blood glucose and insulin levels.[6,24,25] The slight rise in serum creatinine concentration observed early in the course of supplemented fasting probably represents a mild pre-renal state associated with previously demonstrated increased fluid and electrolyte losses that occur shortly after the onset of starvation.[11,20] This was readily reversed with adequate fluid and electrolyte supplementation employed in the present study.

In conclusion, supplemented fasting is safe and effective for rapid weight reduction in exogenous obesity. Side effects are minimal and the therapy is well tolerated. Changes of serum electrolytes noted during the six-week study period were quite mild, and hypokalemia reported with other modalities was not seen with this regimen. Likewise, acidosis and hyperuricemia were generally mild and transient. Beneficial effects observed, other than weight loss, included significant reductions in fasting blood glucose, serum cholesterol, and triglyceride concentrations as well as a decrease in blood pressure.

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